

WHAT IS CLAIMED IS:

1. A primer set that can be used to screen a polynucleotide sample to detect and identify variants in the Cytochrome P450 isoenzyme 2D6 (CYP2D6) gene comprising one or more than one primer group of the three primer groups of sequences selected from the primer groups consisting of Primer Group I (16 or more than 16 consecutive nucleotides of SEQ ID NO:9, 16 or more than 16 consecutive nucleotides of SEQ ID NO:10, 16 or more than 16 consecutive nucleotides of SEQ ID NO:11, 16 or more than 16 consecutive nucleotides of SEQ ID NO:12, 16 or more than 16 consecutive nucleotides of SEQ ID NO:13 and 16 or more than 16 consecutive nucleotides of SEQ ID NO:14); Primer Group II (16 or more than 16 consecutive nucleotides of SEQ ID NO:15, 16 or more than 16 consecutive nucleotides of SEQ ID NO:16; 16 or more than 16 consecutive nucleotides of SEQ ID NO:17, 16 or more than 16 consecutive nucleotides of SEQ ID NO:18, 16 or more than 16 consecutive nucleotides of SEQ ID NO:19, 16 or more than 16 consecutive nucleotides of SEQ ID NO:20, 16 or more than 16 consecutive nucleotides of SEQ ID NO:21, 16 or more than 16 consecutive nucleotides of SEQ ID NO:22, 16 or more than 16 consecutive nucleotides of SEQ ID NO:23 and 16 or more than 16 consecutive nucleotides of SEQ ID NO:24); and Primer Group III (16 or more than 16 consecutive nucleotides of SEQ ID NO:25; 16 or more than 16 consecutive nucleotides of SEQ ID NO:26; 16 or more than 16 consecutive nucleotides of SEQ ID NO:27, 16 or more than 16 consecutive nucleotides of SEQ ID NO:28, 16 or more than 16 consecutive nucleotides of SEQ ID NO:29, 16 or more than 16 consecutive nucleotides of SEQ ID NO:30, 16 or more than 16 consecutive nucleotides of SEQ ID NO:31, and 16 or more than 16 consecutive nucleotides of SEQ ID NO:32).
2. The primer set of claim 1, comprising two primer groups selected from the group consisting of Primer Group I, Primer Group II and Primer Group III.
3. The primer set of claim 1, comprising all three primer groups Primer Group I, Primer Group II and Primer Group III.
4. The primer set of claim 1, where each sequence consists of at least 17 consecutive nucleotides.
5. The primer set of claim 1, where each sequence consists of at least 18 consecutive nucleotides.

6. The primer set of claim 1, where each sequence consists of at least 19 consecutive nucleotides.

7. The primer set of claim 1, where each sequence consists of at least 20 consecutive nucleotides.

5 8. The primer set of claim 1, where each sequence consists of at least 21 consecutive nucleotides.

9. The primer set of claim 1, where one or more than one sequence additionally comprises a tail sequence.

10 10. The primer set of claim 1, where one or more than one sequence has one or more than one dUTP substituted for TTP.

11. A method of screening a polynucleotide sample to detect and identify the presence of one or more than one variant in the CYP2D6 gene in the sample, comprising:

15 a) providing a polynucleotide sample potentially comprising a sequence comprising at least about 50 consecutive nucleotides from one or more than one of the sequences of the wild type CYP2D6*1, SEQ ID NO:1, one or more than one variant of wild type CYP2D6*1, SEQ ID NO:1 or both wild type CYP2D6*1, SEQ ID NO:1 and one or more than one variant of wild type CYP2D6*1, SEQ ID NO:1;

20 b) providing a primer set according to claim 1;

c) amplifying the polynucleotide sample using the provided primer set to produce a set of amplicons; and

25 d) analyzing the amplicons to identify the presence of CYP2D6*1 gene, SEQ ID NO:1, the presence of one or more than one variant of the CYP2D6*1 gene, SEQ ID NO:1 or to identify one or more than one specific variant of the CYP2D6*1 gene, SEQ ID NO:1 in the sample.

12. A method of predicting the potential for altered metabolism of a substance, including one or more than one pharmaceutical drug, by a first individual compared to a second control individual, where the substance is metabolized by the CYP2D6 isoenzyme, and where the second control individual is homozygous for the wild type allele of the CYP2D6*1, SEQ ID NO:1, the method comprising:

30 a) providing a polynucleotide sample from the first individual;

b) providing a primer set according to claim 1;

c) amplifying the polynucleotide sample using the provided primer set to produce a set of amplicons;

d) analyzing the amplicons to detect and identify one or more than one variant in the CYP2D6 gene from the first individual; and

5 e) analyzing the one or more than one variant in the CYP2D6 gene detected and identified to determine if it constitutes a silent variant or non-silent variant;

where the absence of a non-silent variant means that the first individual will not have the potential for altered metabolism of the substance, and where the presence of a non-silent variant means that the first individual will have the potential for altered metabolism of the substance.

13. A method of screening a population to detect and identify the presence of one or more
than one variant in the CYP2D6 gene, comprising:

- a) providing a plurality of polynucleotide samples from the population;
- b) providing a primer set according to claim 1;
- c) amplifying the polynucleotide sample using the provided primer set to produce a set of amplicons; and

d) analyzing the amplicons to detect and identify of one or more than one variant of the CYP2D6*1 gene, SEQ ID NO:1 in the sample.

14. The method of 13, where the plurality of polynucleotide samples is a plurality of random samples of individuals in the population.

20 15. The method of 13, where the plurality of polynucleotide samples is one or more than
one sample from each individual in the population.

16. The method of 13, where the method of screening a population further comprises determining the distribution of the variants in the CYP2D6 gene in the population.

17. The method of 13, where the method of screening a population further comprises
25 recording the presence and identity, or recording the distribution of the variants in the CYP2D6
gene in the population sample, in writing or another suitable media.

18. The method of claim 11, 12 or 13, where the amplifying the polynucleotide sample comprises using modified nucleotides.

19. The method of claim 11, 12 or 13, where the modified nucleotides are selected from the group consisting of deaza dATP, deaza dGTP, and nucleotides labeled with one or more than one label selected from the group consisting of biotin, digoxigenin, and a fluorescent dye.

5 20. The method of claim 11, 12 or 13, where the amplifying the polynucleotide sample comprises using dUTP in place of TTP.

21. The method of claim 11, 12 or 13, where the amplification step is performed in two stages.

22. The method of claim 11, 12 or 13, where analyzing the amplicons is performed using a method selected from the group consisting of dideoxy sequencing, pyrosequencing and SSCP.

10 23. A kit for screening a polynucleotide sample to detect and identify the presence of one or more than one variant in the CYP2D6 gene in the sample, comprising suitable amounts of a primer set according to claim 1.

15 24. The kit of claim 23, further comprising one or more than one additional reagent or one or more than one vessel to amplify the polynucleotide sample, to analyze the amplicons, or both to amplify the polynucleotide sample and to analyze the amplicons.

25 25. The kit of claim 24, where the additional reagent is selected from the group consisting of one or more than one DNA dependent polymerase, one or more than one buffer, one or more than one detergents and one or more than one stabilizing agent.

20 26. A purified or isolated variant of SEQ ID NO:1 having one or more than one of the alterations selected from the group consisting of C>T at position 1522, G insert at position 1576, G>C at position 1851, A>C at position 1852, A>G at position 1864, T>A at position 3230, C>T at position 3232, G>A at position 3335, C>T at position 3542, T>C at position 3617, A>G at position 3716, C>T at position 3922, G>T at position 4221, G>A at position 4280, G>A at position 4282, T>A at position 4379, T>C at position 4555, G>A at position 4607, 25 C>T at position 4820, A>G at position 4854, T>C at position 4873, insertGT at position 4878, C>A at position 5003, T>C at position 5027, C>A at position 5054, C>T at position 5409, G>A at position 5496, C>T at position 5774, C>T at position 5791, C>T at position 5948, C>T at position 6020 and an exon 9 gene conversion.

30 27. A method of predicting the potential for altered metabolism of a substance, including one or more than one pharmaceutical drug, by a first individual compared to a second control

individual, where the substance is metabolized by the CYP2D6 isoenzyme, and where the second control individual is homozygous for the wild type allele of the CYP2D6*1, SEQ ID NO:1, the method comprising:

- 5 a) detecting and identifying one or more than one variant in the CYP2D6 gene from the first individual; and
- b) analyzing the one or more than one variant in the CYP2D6 gene detected and identified to determine if it constitutes one or more than one variant according to claim 26;

where the presence of the one or more than one variant means that the first individual will have the potential for altered metabolism of the substance.

10 28. A purified or isolated variant of SEQ ID NO:3 having one or more than one of the alterations selected from the group consisting of F>I at position 120, F>F at position 120, E>K at position 155, R>R at position 194, F>F at position 219, L>L at position 276, H>H at position 324, R>STOP at position 344, Y>C at position 355, H>H at position 361, V>FRAMESHIFT at position 363, E>K at position 418, H>Y at position 478, F>F at position 15 483.

20 29. A method of predicting the potential for altered metabolism of a substance, including one or more than one pharmaceutical drug, by a first individual compared to a second control individual, where the substance is metabolized by the CYP2D6 isoenzyme, and where the second control individual is homozygous for the wild type allele of the CYP2D6*1, SEQ ID NO:1, the method comprising:

- 25 a) detecting and identifying one or more than one variant in the CYP2D6 isoenzyme from the first individual; and
- b) analyzing the one or more than one variant in the CYP2D6 isoenzyme detected and identified to determine if it constitutes one or more than one variant according to claim 28;

where the presence of the one or more than one variant means that the first individual will have the potential for altered metabolism of the substance.